be a reliable, sensitive technique in the literature, that fact is of little use if the procedure is either not available or subject to substantial technical-interpretive limitations when requested from a specific diagnostic service in a specific hospital.

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Pulmonary Reactions to Drug Therapy

THE REACTIONS of pleuropulmonary tissues to drugs are increasing both in number and in variability of presentation. Although the mechanism involved in these reactions remains speculative, certain pharmacologic agents are more commonly associated with pathological conditions of the lungs.

Nitrofurantoin, a widely prescribed antibacterial agent, has been known for many years to cause both acute and chronic interstitial lung disease, pleural effusion and the pulmonary infiltrate with eosinophilia (PIE) syndrome. Recently, Bone and colleagues described the cases of two patients in which nitrofurantoin therapy was linked to the formation of desquamative interstitial pneumonitis. This disease may present as a predominantly alveolar pattern on roentgenograms of the chest. Both of their patients improved on discontinuance of the drug plus administration of corticosteroids. This reemphasizes the excellent prognosis for patients in whom the clinical entity of nitrofurantoin induced lung disease is recognized and the drug is discontinued.

A second widely prescribed drug, phenytoin (diphenylhydantoin), similarly has been shown to produce a variety of pulmonary reactions. Hilar adenopathy, acute and chronic interstitial lung disease, as well as miliary infiltrates all have been reported.

Hazlett has studied the loss of lung function occurring in patients receiving long-term phenytoin therapy. In 45 percent of their patients there were reduced steady-state diffusing capacities (DL_{CO}) and abnormal blood gas tensions for oxygen during exercise. In addition, in 50 percent of their patients there were widened resting alveolar-arterial oxygen differences or no increases in DL_{CO} with exercise, or both. The disturbing frequency of abnormalities, especially in younger patients, emphasizes the need to consider physiologic monitoring in order to follow and possibly prevent irreversible pulmonary disease in patients taking phenytoin.

Chemotherapy with cytotoxic drugs also is associated with pulmonary injury. Cytotoxic drug-induced lung disease, including both acute and chronic interstitial disease, hilar adenopathy, alveolar disease, pleural disease and lung carcinogenesis all have been reported. Methotrexate, busulfan and bleomycin have been the most commonly associated cytotoxic drugs.

Bleomycin, a drug with no major toxic effects on bone marrow or lymphoid tissue, has been known to cause interstitial pneumonia and pulmonary fibrosis in between 3 and 6 percent of patients. It is rarely seen in doses below 200 mg but death from pulmonary toxicity has been recorded in as many as 10 percent of patients who have received more than 550 mg. Therefore it would seem prudent to withdraw administration of the drug when symptoms, roentgenographic abnormalities or significant changes in pulmonary function occur. If infection is excluded and findings on pulmonary biopsy indicate bleomycin toxicity, the drug should be permanently discontinued.

Alarcon-Segovia has categorized drugs capable of inducing the development of systemic lupus erythematosus (SLE). Hydralazine, procainamide, phenytoin, isoniazid and chlorpromazine are among the drugs capable of inducing SLE in many persons receiving them for some time. In general, the clinical features of drug-induced SLE differ little from those of spontaneously occurring disease. However, pulmonary disease is much more common with the former.

Procainamide, an antiarrhythmic agent, and hydralazine, an antihypertensive agent, both widely prescribed, may produce pleuropulmonary disease. Indeed, 30 percent of patients with procainamide-induced SLE present with pleurisy whereas only 2.5 percent of spontaneously occurring SLE have symptoms referable to the lung. Additionally, serological differences also are present. Antinative deoxyribonucleic acid (DNA) antibodies do not occur in procainamide-induced

disease but have been reported with hydralazine-induced SLE. Discontinuance of these drugs has been associated with a high percentage of reversibility of disease.

Recognition that pulmonary injury may be secondary to many drugs is of great importance in preventing patient morbidity and mortality.

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The Staging of Lung Cancer: Clinical Benefits

TUMOR STAGING evaluates tumor size and location, the absence or presence and extent of lymph node or systemic metastasis, and tumor cell type. The techniques for staging lung cancer include physical examination, chest roentgenograms with hilar and mediastinal tomography, sputum cytology and isotopic scans. Bronchoscopy and mediastinoscopy are surgical methods for staging bronchogenic carcinoma.

The first benefit derived from staging has been the elimination of the unnecessary physical, emotional and financial cost of thoracotomy when that operation will not be beneficial. Therefore, patients with oat cell (small cell undifferentiated) carcinoma or contralateral mediastinal metastasis, whose survival will not be enhanced by surgical operation on the chest, are treated by other means.

The data from prospective and retrospective staging studies are beginning to aid clinicians in choosing and timing other forms of therapy for lung cancer. McKneally has done a randomized prospective study of patients with stage I tumors treated by resection and followed from one to three years. There were nine recurrences with death among the control group of 25 patients. Of 19 patients who were given intrapleural bacille Calmette Guérin (BCG) immunotherapy in the immediate postoperative period, there was only one patient with recurrence of tumor in the same period and all patients survived. Patients identified to have stage III lung cancer are showing improved survival with a combination of radiotherapy and multiagent chemotherapy (cyclophosphamide (Cytoxan®), doxorubicin hydrochloride (Adriamycin®), methotrexate and procarbazine).

How extensive should staging efforts be? In a patient with advanced lung cancer, x-ray studies of the chest, physical examination, and evaluation of symptomatic disease and immunocompetence (denitrochlorobenzine [DNCB] skin test) should suffice. For patients with malignancy in more confined stages, a group of informed and concerned cancer therapists should apply uniform diagnostic and treatment methods in the best known manner.

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